UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/780,904	02/17/2004	Lorraine D. Butlin	IMIN.P-033-2	7556

21121 7590 09/03/2004

OPPEDAHL AND LARSON LLP
P O BOX 5068
DILLON, CO 80435-5068

EXAMINER	
PORTNER, VIRGINIA ALLEN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 09/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/780,904	BUTLIN ET AL.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/2/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *15,16 and 18-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *15 and 16* is/are allowed.

6)☐ Claim(s) *18-30 and 33-37* is/are rejected.

7)☐ Claim(s) *20,22 and 31-34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 15-16, 18-37 are pending.

Allowable Subject Matter

1. Claims 15 and 16 define over the prior art of record and are therefore allowed.

Response to Arguments

2. Applicant's arguments with respect to claims 18 and dependent claims therefore have been considered but are moot in view of the new ground(s) of rejection.

Claim Objections

3. Claims 22, and 31-32 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

a. Claim 22 depends from claim 21 and recites a wherein clause that defines the "first antibody pair detects total FSH". The clause does not set forth a methods step, reagent or characteristic that is encompassed by the first and second antibody pairs recited in claim 21. Both antibody pairs of claim 21 would detect total FSH as they bind to the alpha and beta peptides in an assay that requires both antibodies for carrying out the assays. To have an antibody pair that binds both the alpha and beta peptide chains, and not a differentiating carbohydrate epitope or mutant form of FSH, would detect Total FSH. Therefore Claim 22 does not further limit claim 21.

b. Claims 31 and 32 depend from a canceled claim 1 and therefore do not further limit the claim from which they depend.

4. Claims 20 and 33-34 are objected to because of the following informalities:

c. Claim 20 recites the phrase "claim 19;", the semi-colon ":", should be a comma.

d. Claim 33 recites the phrase "independent of the whether the"; there is one too many articles recited. This objection could be obviated through removal of the first appearing [the] in this phrase.

e. Claim 34 recites the phrase "depending on the whether the"; there is one too many articles recited. This objection could be obviated through removal of the first appearing [the] in this phrase.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 21, 23-25, 29, 31-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 21-25 define the first and second assays to be FSH assays, that assay the presence of FSH with first and second antibody pairs which inturn are defined to bind to the alpha and beta "pepide chains" of FSH, wherein the members of each antibody pair are not the same antibodys. In light of the binding specificity of the antibody pairs being defined to be specific for the alpha and beta peptide chains of FSH, both assays measure the exact same indicator.

Claims 21-25 depends from claim 18 which requires the first assay to assay an indicator that is independent of menopausal status and the second assay to measure an indicator of menopausal status. In light of the fact that both assays of claims 21-25 bind to the same or equivalent indicator FSH, and each antibody is specific for the same or equivalent peptide chain, claims 21-25 set forth a combination of claim limitations that is not internally in agreement with the requirements of the assay steps of independent claim 18 through reciting a combination of claim limitations that are not internally consistent with step 18 (b). While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

8. Claim 23 determines the ratio of the first and second FSH assays that use different first and second antibodies directed to that alpha and beta peptide chains of FSH. While determining the ratio is clear, how a number divided by itself provides an indication of menopausal status is not clearly pointed. The assay using the two sets of antibodies are not distinguished, the amount of FSH determined is assumed to be the same and a number divided by itself is equal to 1. A ratio of 1 does not provide any insight into menopausal status. While the specification can be used to provide definitive support, the claims are not read in a vacuum. Rather, the claim must be definite and complete in and of itself. Limitations from the specification will not be read into the claims. The claims as they stand are incomplete and fail to provide adequate structural properties to allow for one to identify what is being claimed.

9. Claims 24-25 repeat the two contemporaneous assays after an interval of at least one week, on the same sample of claim 21, to determine if the menopausal status of the female individual is changing. The indication the sample gave on first assay, which is then reassayed on the same sample "at least one week" later, should give a result that is the same or equivalent to the first assay and the menopausal status of the individual would not change. Values for FSH increase with on set of menopause. A sample frozen and tested at a future date would give the same or lower value for FSH due to loss of activity from the freeze thawing process. Something is missing from the claimed method.

Claim 29 is unclear for reciting a combination of claim limitations that is not consistent with Applicant's definition of the term "contemporaneous". The definition of the term "contemporaneous" at page 8, lines 12-27 defines this term to include: Samples that have been sub-divided into multiple portions obtained from the same individual, or more than one sample obtained from the same individual on the same day, within a couple of hours of each other. Claim 29 depends from claim 18(independent claim), and recites "further comprising the step of repeating the two contemporaneous assay after an interval of at least one week to determine is menopausal status of the human female individual is changing". Claim 18 recites "the same sample obtained from step a", which in combination with the newly submitted claim limitations of claim 29 produces a lack of clarity as to what sample is being analyzed that would meet the definition of contemporaneous samples. Claim 29 appears to be analyzing the "same sample" set forth in claim 18, but the sample of claim 18 is greater than or equal to "at least one week" old; this is not the definition of "contemporaneous set forth in the instant specification.

Claims 31-32 depend from canceled claims and are therefore incomplete and unclear with respect to the meets and bounds of the claims.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 18-20, 33-37 are rejected under 35 U.S.C. 102(b)as being anticipated by O'Daly et al (US Pat. 5,391,272).

Instant claims 18-20 33: O'Daly et al disclose the instantly claimed invention directed to a device and method (see Example 7, Figures 12(FSH) and 13 (LH) sandwich format) of use, the device comprising:

(a) a first gonadotropin-responsive signal producing means, that relative to a reference standard produces a signal indicative of the gonadotropin present in the sample that is

independent of whether the human is pre-menopausal or post-menopausal (see col. 20, lines 25-59).

(b) a second gonadotropin-responsive signal producing means, that relative to a reference standard produces a signal indicative of the gonadotropin present in the sample that is different depending on whether the human is pre-menopausal or post-menopausal (see col. 19, lines 25-68, and col. 20, lines 1-23).

(c) means for combining the signals produced (spectrophotometric assay (see col. 20, lines 37-38 and claims 20-47 (electrode surface)).

Instant claim 34: signals produced indicative of FSH (see "colloidal gold adsorbed anti-FSH (see claims 29-30) together with an "enzyme/antibody conjugate).

Instant claim 35: "produce a signal as a result of binding in a detection zone (electro-immunosensor") of a labeled specific binding reagent with a particulate direct label ("colloidal gold adsorbed anti-analyte antibodies; col. 20, Example 7)

Instant claim 36: wherein the antibody is directed to the alpha or beta peptide chains of FSH (see col. 20, lines 35-35).

Instant claim 37: each signal means produce a signal (two signals are generated for each analyte, specifically the colloidal gold (first signal means) and enzyme label (second signal means) for FSH, and two signal are generated for LH, specifically the colloidal gold (first signal means) and different second enzyme label (second signal means) (see Example 7 and all device claims). The reference anticipates the instantly claimed invention.

12. Claims 18-20,26-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Overlie, I et al (1999).

Overlie, I et al disclose the instantly claimed invention directed to a method of testing a human female individual to determine if the human female is pre-menopausal or post-menopausal, the method comprising the steps of:

Obtaining a gonadotropin containing sample (see page 643, col. 1, "venous blood", last paragraph and "serum" col. 2, paragraph 1),

Performing contemporaneous first and second assays (FSH, LH, E2, PRL,TSH, Progesterone, testosterone see "Hormone and Protein analyses", "two different epitopes on the antigen" page 643, col. 2, paragraph 3, two polyclonal antibody assays to the alpha and beta peptide chains) on the sample,

wherein the first assay measured a first indicator, specifically total progesterone and testosterone using a polyclonal antiserum (see page 643, col. 2, paragraph 5) and

wherein the second assay differentiates premenopause and postmenopausal levels of hormone (see Table II, page 644, bottom of page)

Comparing (time comparisons (see Table II ledger) and ratios of FSH/LH (see page 644, col. 2, paragraph 2, last sentence and Fig. 1; page 645, col. 2, paragraph 2-3 "At the menopause the endocrine picture is characterized by high gonadotropins and low sex steroid levels and an increased ratio E1/E2")) the results of the first and second assays to determine if the human female individual is pre-menopausal or post-menopausal. The reference anticipates the instantly claimed invention.

13. Claims 18,26-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Birken et al (US Pat. 6,521,416)

Birken et al disclose the instantly claimed invention directed to a method of testing a human female individual to determine if the human female is pre-menopausal or post-menopausal, the method comprising the steps of:

Obtaining a gonadotropin containing sample (see col. 11, lines 1-2 "urine"; "blood, col. 18, lines 24-25),

Performing contemporaneous first and second assays (samples taken at time intervals over the course of a day (see Table VI, col. 26), as well over a period of at least two consecutive days (see col. 10, lines 44-51); col. 13, lines 57-67 and col. 14, lines 1-19) on the sample,

wherein the first assay measured a first indicator (see hLh, HLHB, hLHBcf and hCGcf (see col. 23, lines 18-55) and col. 14, lines 16-19;),and

wherein the second assay differentiates premenopause and postmenopausal levels of hormone (see col. 3, lines 15-22; see col. 4, lines 1-13)

Comparing determined values and ratios (see col. 6, lines 60-67) the results of the first and second assays to determine if the human female individual is pre-menopausal or post-menopausal (see col. 20, Table IV; col. 28, lines 34-36).

Instant claim 26: first and second sandwich assays (see col. 9, lines 50-55; col. 22, lines 34-67; col. 23).

Instant claim 27: two different antibody pairs to the alpha (anti-A, LH-1 and LH-2, see col. 18, lines 54-67) and beta subunits (see Table III, anti-B (LHB) and monoclonal antibodies col. 3, lines 39-65)

Instant claim 28: ratio of results (see col. 6, lines 64-67; col. 27, Example 4, lines 32-46).

Instant claim 29: an interval of at least one week (five or more consecutive days, col. 12, line 5; days 1 through day 10 (see col. 16, lines 1-5; col. 27, lines 32-36), 60 day random collection (see col. 16, lines 32-36)

Instant claim 30: female under going hormone replacement therapy (see col. 12, lines 18-44)

The reference anticipates the instantly claimed invention.

14. Claims 18, 26-27 are rejected under 35 U.S.C. 102(b)as being anticipated by Niccoli et al (1996) as evidenced by Costagliola et al (1994, reference 13, incorporated by reference).

Instant claim 18 Niccoli et al disclose the instantly claimed invention directed to a method of testing a human female individual to determine if the human female is pre-menopausal or post-menopausal, the method comprising the steps of:

Obtaining a gonadotropin containing sample (see Table 1, page 745, "normal women", "normal women (stimulated)" which would include hormone replacement therapy, "postmenopausal woman"),

Performing contemporaneous first and second assays (assays A-L) on the sample,

wherein the first assay measured a first indicator (total lutropin (assay I, polyclonal, page 742, Figure 2, and evidence provided by Costagliola et al)and

wherein the second assay differentiates pre-menopause and post-menopausal levels of hormone (Assays are two site sandwich assays, see page 742, col. 2, first paragraph,)

Comparing (see pages 745 and 746) the results of the first and second assays (Tab. 1 compares the assay results) to determine if the human female individual is pre-menopausal or post-menopausal.

Instant claim 26: wherein the first and second assays are sandwich format assays (see page 746 narrative at top of page (and evidence provided by Costagliola et al, page 414, Figure 4).

Instant claim 27: wherein the first assay makes use of a first antibody pair directed to the alpha and beta peptide of the gonadotropin (assay E), and a second antibody pair directed against the alpha and beta peptide chains of the gonadotropin, wherein both members of the first antibody pair are different from the members of the second antibody pair (see page 745, column 2, 55 monoclonal antibodies, for 21 different epitopes and page 746, col. 2, "None of the kits were strictly identical with regard to the epitope specificity of the monoclonal antibodies used ").

The reference anticipates the instantly claimed invention.

Conclusion

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

16. Ching et al (US Pat. 5,780,308) disclose the invention of claims 33 and 37 (see col. 15-16, "HCG", col. 6, lines 16-63, col. 7-8 and all claims.

17. Clough et al (US Pat. 5,366,863) is cited to show assay methods for measurement of total gonadotropin alpha peptide in urine (see col. 2, lines 1-67 and entire document.)

18. Ala-Fossi et al (1998). disclose the instantly claimed invention directed to a method of testing a human female individual to determine if the human female is pre-menopausal or post-menopausal, the method comprising the steps of:

Obtaining a gonadotropin containing sample (see blood samples obtained, see page 240, col. 2, last paragraph,

Performing contemporaneous first and second assays on the sample

wherein the first assay measures an analyte that is independent of menopausal state (standard curve for hormones, see section 2.2, page 241; and "abstract, "Peripheral testosterone level did not increase with age"), and

wherein the second assay differentiates premenopause and postmenopausal levels of hormone (see page 240, col. 2, paragraphs 2, 4 and 5; page 242, Table 1, "Testosterone" column)

Comparing the results of the first and second assays to determine if the human female individual is pre-menopausal or post-menopausal (see table 1, page 2; significant difference in testosterone levels in the ovarian vein samples.

19. Anobile, CJ et al (1998). disclose the instantly claimed invention directed to a method of testing a human female individual to determine if the human female is pre-menopausal or post-menopausal, the method comprising the steps of:

Obtaining a gonadotropin containing sample (see serum(sera) samples, see page 632, col. 1, third paragraph,

Performing contemporaneous first and second assays (FSH, LH, Progesterone, Oestradiol (see Table 1, page 633, top of page) on the sample,

wherein the first assay measures an analyte that is independent of menopausal state ("see Figure 2, page 634, "simple" carbohydrate glycosylation did not change relative to menopausal stage for FSH, relative to the total FSH in the sample), and

wherein the second assay differentiates premenopause and postmenopausal levels of hormone (see Figure 4, the proportion of FSH isoforms (pI>4.3) and LH isoforms eluting with a pI >6.55 showed a significant difference relative to premenopause samples and therefore differentiated menopausal state.)

Comparing the results of the first and second assays to determine if the human female individual is pre-menopausal or post-menopausal (see page 637, col. 2, paragraph 3).

20. Creus, S et al (1996). disclose the instantly claimed invention directed to a method of testing a human female individual to determine if the human female is pre-menopausal or post-menopausal, the method comprising the steps of:

Obtaining a gonadotropin containing sample (see serum samples, page 182, Materials and Methods section),

Performing contemporaneous first and second assays (FSH, Progesterone, Oestradiol (see Table 1, page 184, top of page) on the sample,

wherein the first assay measured total protein patterns (see Figure 1, page 184, bottom of page),and

wherein the second assay differentiates premenopause and postmenopausal levels of hormone (see Figure 4, the proportion of FSH isoforms (pI>4.3) and LH isoforms eluting with a pI >6.55 showed a significant difference relative to premenopause samples and therefore differentiated menopausal state.)

Comparing the results of the first and second assays to determine if the human female individual is pre-menopausal ("FPS", follicular phase) or post-menopausal (PMS "menopause", see Table 1, significant difference in immunological, biological and ratio of FSH levels in the sample relative to pre- and post- menopausal stage).

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on 7:30-5:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
August 26, 2004

L. R. F. Smith
LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600